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Formulation of Different Polymer Coated Spherules from Granules

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Abstract:
A novel spheronisation technique is reported here for forming spherules from granules using FDA approved excipients and common pharmaceutical unit operations. The aspirin is used as a model drug to check stability during the process. For that, spherules are prepared by "bed coating during sliding" (BCDS) of granules. Spherules with two size range (sieve no 20 and 30) are compared.

These spherules are further coated with polymers to show the versatility of the process. flow property determination. Angle of Repose sand packing parameters appeared excellent. Different polymer coating gives different release profile as per the properties of the polymer. However, the drug content is lower for 30 as compared to 20 while drug release profile appears similar. This is a robust and versatile platform delivery system for developing advanced drug delivery systems (ADDS).

Keywords: Spherules, Granulation, Spheronization, Bed coating during sliding(BCDS), Advanced drug delivery system(ADDS), fluidised bed drying(FBD)

INTRODUCTION:

Spheronization is the most widely used method of manufacturing spherules (spherical shaped particles) [1, 2]. Which produces spherules with high drug loading capacity and better flow properties as compared to granules and pellets [3, 4]. This is because in granules and pellets the shape is not necessarily spherical in nature [5, 6]. The spherules in addition provides an opportunity to modify its surface properties by polymer film coating [7]. Surface coatings improve the functional properties such as appearance, drug release and integrity of particles during processing of spherules [8, 9]. As compared to granules, spherules have low surface area to volume ratio so less amount of coating solution is required [10, 11].

Spheronization is generally done with fluidised bed drying (FBD) [12], where the droplets are dried in air under circulation produce spherules with irregular shape and surface roughness due to rapid drying. Thus, alternative methods are required that can be adopted in small and large process to produce uniform spherules.

Low-cost production of spherules can be achieved by wet granulation followed by "bed coating during sliding (BCDS)" as these processes can be engineered to regular pharmaceutical unit operations and scaled up [1]. Granulation can be done by sieving followed by sizing [13]. The spheronization by BCDS can lead

to uniform sized particles as polishing of coated starch particles to granules are happening during sliding, that can lead to conversion of granules to spherules. The spherules can be surface modified by polymer film coating [14]. Polymers with different physical properties can be used for that purpose. Ethyl cellulose (EC), is a cellulose derived polymer, During coating color and appearance of the spherules are being changed using appropriate colors and excipients [21].While this process appears affordable and accessible for small and large scale processes, it can lead to disadvantages as well. For example, the wet process can affect the stability of drug molecule.

In the current study, the effect of wet granulation, BCDS and polymer coating on stability of aspirin is analysed. The granules, spherules and coated spherules are successfully prepared.

AIM: Formulation of different polymer coated spherules from granules

OBJECTIVES:
A novel spheronisation techniques is reported here for forming spherules from granules using FDA approved excipients and common pharmaceutical unit operations.

METHOS AND PREPERATION:
1. Ingredient:
Aspirin: -
Aspirin is belonging to the class of NSAID having analgesic, antiplarytic. Anti- inflamentry anti-platelete activity at symentric standard dose.

Lactose:
Lactose is one of the most commonly used excipients within the pharmaceutical industry in the production of solid dosage. Lactose is commonly used as a diluent/binder in order to produce tablets of sufficient hardness whilst maintaining good disintegration properties

Starch Powder:
Aside from their basic nutritional uses, starches are used in brewing and as thickening agents in baked goods and confections. Starch is used in paper manufacturing to increase the strength of paper and is also used in the surface sizing of paper.

Ethyle cellulose:
Ethylcellulose is used in pharmaceutical technology as a coating agent, flavoring fixative, binder, filler, film-former, drug carrier, or stabilizer

Ethanol:
Ethanol is present in alcoholic drinks (beer, wine, spirits) when diluted. It is used as a topical agent to prevent skin infections, in pharmaceutical preparations (e.g. rubbing compounds, lotions, tonics, colognes), cosmetics, and in perfumes

Aspirin	12gm
Lactose	0.012gm
Starch Powder	0.16gm
Ethyle cellulose	1gm
Ethanol	100ml

METHODOLOGY:

Wet granulation of aspirin granules was done by anestablished procedure [22]. For that, aspirin (12gm), lactose
(6mg) and starch powder (80mg) were taken in a mortar and pestle, ground it into fine powder. Then starch paste (5% w/v) was added and mixed well to form coherent mass. The coherent mass were passed through sieve no.12 to get wet granules [13, 23].

Preparation of polymer coated spherules

Wet granules (10gm) was accurately weighed and taken into 250ml beaker and rotated in clockwise direction at 45° angle. While rotating ethanol: water (50:50 v/v) mixture were sprayed to granule bed for maintaining the wetness. Small amount of starch powder was added while rotating, to improve the flow properties and 6-7 drops of starch solution (prepared by adding 3 drops of 5% starch paste in 7ml distilled water) are also added or sprayed to this rotating granule bed for improving the binding of small fines of starch powder to get the spherules. The prepared spherules were then sieved (sieve no 20 and 30) to get uniform sized spherules. Coating solution were prepared by dissolving polymer (500 mg),saffron and talc (400 mg) dissolved in acetone (25 ml). Coating solution were sprayed to the spherule bed with constant rotation. After coating the spherules were spread on petridish and kept at 60 C in hot air oven for 20 min to prepare dried polymer coated spherules.

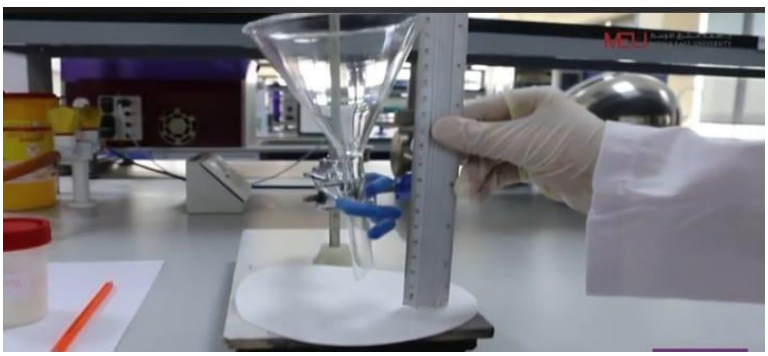
Microscopical evaluation of spherules and granules

The shape and surface properties of granules and spherules were examined using a projection microscope. The prepared spherules and granules were separately taken in a glass slide and kept under projection microscope (10x) to observe the shape and edges of particles. Randomly selected 15 particles were studied for its shape. Particles were analysed by counting the number of edges 45^0, 90^0, 120^0 in each particles were collected and analysed using projection microscope

Angle of Repose (tan θ) = h/r

Where 'h' is the height and 'r' is the radius of pile. The flow pattern of different AR is as follows; excellent (25-30), good (31-35), fair (36-40), passable (41-45), poor (46-55), very poor (56-65) and >66 represents very very poor flow property [24, 25, 26, 27].

www.fabricatorguide.com	tangent table tan theta 1° degree to 45° degree								
1°	0.01745	10°	0.17632	19°	0.34432	28°	0.53170	37°	0.75355
1.5°	0.02618	10.5°	0.18533	19.5°	0.35411	28.5°	0.54295	37.5°	0.76732
2°	0.03492	11°	0.19438	20°	0.36397	29°	0.55430	38°	0.78128
2.5°	0.04366	11.5°	0.20345	20.5°	0.37388	29.5°	0.56577	38.5°	0.79543
3°	0.05240	12°	0.21255	21°	0.38386	30°	0.57735	39°	0.80978
3.5°	0.06116	12.5°	0.22169	21.5°	0.39391	30.5°	0.58904	39.5°	0.82433
4°	0.06992	13°	0.23086	22°	0.40402	31°	0.60086	40°	0.83909
4.5°	0.07870	13.5°	0.24007	22.5°	0.41421	31.5°	0.61280	40.5°	0.85408
5°	0.08748	14°	0.24932	23°	0.42447	32°	0.62486	41°	0.86928
5.5°	0.09628	14.5°	0.25861	23.5°	0.43481	32.5°	0.63707	41.5°	0.88472
6°	0.10510	15°	0.26794	24°	0.44522	33°	0.64940	42°	0.90040
6.5°	0.11393	15.5°	0.27732	24.5°	0.45572	33.5°	0.66188	42.5°	0.91633
7°	0.12278	16°	0.28674	25°	0.46630	34°	0.67450	43°	0.93251
7.5°	0.13165	16.5°	0.29621	25.5°	0.47697	34.5°	0.68728	43.5°	0.94896
8°	0.14054	17°	0.30573	26°	0.48773	35°	0.70020	44°	0.96568
8.5°	0.14945	17.5°	0.31529	26.5°	0.49858	35.5°	0.71329	44.5°	0.98269
9°	0.15838	18°	0.31529	27°	0.50952	36°	0.72654	45°	1
9.5°	0.16734	18.5°	0.33459	27.5°	0.52056	36.5°	0.73996	45.5°	1.0355



Particle packing parameters:

Bulk density is mainly used to find out the uniformity of spherules. That helps to conform size of container, closures, capsules, selection of production apparatus and equipment's.

For that, spherules (20gm) were taken in a 10 ml measuring cylinder were used to find out the bulk density and tapped density. Bulk density was determined by noting down the volume occupied by spherules after tapping manually 2

times on the flat surface. The measuring cylinder containing spherules was attached with a tapped density apparatus and the tapped volume was determined by noting the volume occupied by spherules after 100 tappings on a flat table top. Bulk and tapped density were calculated from bulk and tapped volume by the following formula.

Bulk density = Spherule weight/ Bulk volume Tapped density = Spherule weight/ tapped volume

Compressibility Index or Carr′s Index is the measure of tendency of spherules to consolidate, based on interparticulate interactions. It is estimated by below formula,

Carr′s index = [Tapped density-Bulk density/Tapped density] 100

Carr′s index control values are excellent flow (<10), good (11-15), fair(16-20), passable(21-25), poor(26-31), verypoor (32-37), and very very poor (>38).

Hausner′s Ratio is the ratio of tapped and bulk density. Low values indicate good flow property of spherules.

Hausner′s ratio = Tapped density/Bulk density Hausner′s ratio control values are excellent (1.0 – 1.11),good (1.12-1.18), fair (1.19-1.25), passable (1.26-1.34),poor(1.35-1.45), very poor(1.461.59) and very very poor(>1.60) [25, 26, 27].

Table: 1 Angle of Repose, Bulk density, Tapped density, Carr′s Index and Hausner′s Ratio of Spherules

Spheru les	Angle of Repose (°)	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr′s Index (%)	Hausner′s Ratio
Ethyl cellulose *--*coated spherules retained in sieveNo.20	21.8	0.49	0.5	2	1.02
Ethyl cellulose coated spherules retained in sieveNo.30	26.57	0.49	0.52	5	1.06

RESULT AND DISCUSSION:

The granulation followed by bed coating during sliding (BCDS) with starch leads to the formulation of spherules which is further coated with functional polymers. The spherules are then sieved to obtain 2 different population of uniformly sized spherules (sieve no 20 and 30). In this study the effect of spherionization on flow properties.

CONCLUSION:

Aspirin loaded spherules and coated spherules are successfully prepared from granules by bed coating during sliding (BCDS) process and the flow properties, surface angles, drug content, drug release are optimized. The resulting spherules and the coated spherules are having smooth spherical shape with maximum obtuse angle indicating the spherionization process is successful. The spherules exhibited excellent flow property useful for its manufacturing fidelity.

REFERENCE:

1. Muley S., Nandgude T., Poddar S., Extrusion–spheronization a promising pelletization technique: depth review, *Asian Journal of Pharmaceutical Sciences*. 2016, *11 (6),* 684-699
2. Sinha V.R., Agarwal M.K., Agarwal A., Singh G., Ghai D., Extrusion- spheronization: process variables and characterization, *critical reviews in therapeutic drug carrier systems*. 2009, *26 (3),* 275-331.
3. Soltanbeigi B., Podlozhnyuk A., Jin Y. Ooi., Kloss C., Papanicolopulos S.A., Comparison of multisphere and superquadric particle representation for modelling shearing and flow characteristics of granularassemblies, *EPJ Web Conf*. 2017, *140*, 1-4.
4. Zoubari G., Ali R., Dashevaskiy A., Water soluble and insoluble polymers as binder for pellet preparation by extrusion/ spherionization, *JDDST*. 2019, *49*, 1-5.
5. Lau C.L.S., Yu Q., Lister V.Y., Rough S.L., Wilson D.I, Zhang M, The evolution of pellet size and shape during spheronisation of an extruded microcrystalline cellulose paste, *Chemical Engineering Research and Design.* 2014, *92*, 413–424.
6. Parkin J., Widjaja K.S., Bryan M.P., Rough S.L., Wilson D.I., Experimental validation of a dimensional analysis of spheronisation of cylindrical extrudates, *Powder Technology*. 2016, *298*, 73-83.
7. Basak S. C., Kaladhar K., Doxycycline hyclate delayed release capsules with sodium starch glycolate as a pH- dependent pore forming agent, *Indian J. Pharm. Sci*. 2004, *66*, 704–707.
8. Kablitz C. D., Urbanetz N.A., Characterization of the film formation of the dry coating process, *Eur. J. Pharm. Biopharm*. 2007, *67*, 449–457.
9. Ramlakhan M., Wu C.Y., Watano S., Dave R.N., Pfeffer R., Dry particle coating using magnetically assisted impaction coating: Modification of surface properties and optimization of system and operating parameters,
10. *Powder Technol*. 2000, *112*, 137–148.
11. Bhaskaran S., Lakshmi P. K., Extrusion spheronization –a review, *Int.J. PharmTech Res*. 2010, *2 (4),* 2429-2433.

12. Kamata T., Wada K., Ichikawa H., Dry pre-coating of active pharmaceutical ingredient with submicron-sized hydroxypropylcellulose in dry granulation using roller compactor improves granule properties, *JDDST*. 2017, *453*, 1-24.
13. Pisek R., Sirca J., Svanjak G., Srcic S., Comparison of rotor pelletization (fluid bed) and extrusion/spherionization method for pellet production, *drugs made in Germany.* 2011, *63 (11),* 1202-1209.
14. D'cruz D., Ajith A., Subburaj T., Kamalasanan K., Magnesium stearate is an incompatible excipient for aspirin in wet granulation producing non- linear degradation, *Int J Pharm Sci Res*. 2018, *10 (2),* 240-242.
15. Link K. C., Schlunder E. U., Fluidized bed spray granulation investigation of the coating process on a single sphere, *Chemical Engineering and Processing.* 1997, *36*, 443–457.
16. Goswami K., Khurana G., Marwaha R.K., Gupta M., Development and evaluation of extended release ethylcellulose based matrix tablet of diclofenac sodium, *Int J Pharm .Pharm Sci*.2014, *6 (6),* 296-301